REMARKS

The Official Action mailed March 23, 2004, and the prior art relied upon therein have been carefully reviewed. The claims in the application are now claims 1-16, and these claims define patentable subject matter warranting their allowance. The applicants hereby respectfully request favorable reconsideration and allowance.

Acknowledgement by the PTO of the receipt of applicants' papers filed under §119 is noted.

Claims 1-14 have been rejected under the second paragraph of §112 as being allegedly indefinite. This rejection is respectfully traversed.

Respectfully, this rejection is unjustified. It is well known in the art that divalent cations, such as Ca^{++}, Mg^{++} and Zn^{++}, are required for some enzymatic activities. The art available provides sufficient information to enable those skilled in the art the tools for determining whether, for the purpose of conducting the method of the invention, the addition of a divalent cation is necessary or desirable.

For example, it is known from the art that, *inter alia*, phospholipase A2 and phospholipase D are Ca^{++}-dependent. In addition, it is known from the art that phospholipase C is Ca^{++}-dependent as well as Mg^{++}-dependent, depending on the cell

type. Applicants enclose herewith some, among numerous available, exemplary publications, i.e. abstracts of Bz et al (two abstracts), Reynolds et al, Chien et al and Lindahl et al (five abstracts in total), which discuss divalent cation dependency of phospholipase A2, phospholipase C.

Thus, it is not at all unclear when the enzyme will require a divalent metal cation, as this is well known from the prior art. As stated long ago by the Supreme Court of the United States in *Loom Co. v. Higgins*, 105 US 580, 586 (1881),

> He [the applicant or patentee] may begin at the point where his invention begins, and describe what he has made that is new, and what it replaces of the old. That which is common and well known is as if it were written out in the patent and delineated in the drawings.

To have it any other way would make the content of a patent specification impossibly prolix. As stated in *Spectra-Physics, Inc. v. Coherent, Inc.*, 3 USPQ2d 1737, 1743 (Fed Cir 1987), the specification "need not teach, and preferably omits, what is well known in the art."

As those skilled in the art would fully understand when the presence of a divalent metal cation would be needed or would be helpful, and could even check by routine experimentation is necessary, the criticized recitation of claim 1 is not indefinite.

Applicants respectfully request withdrawal of the rejection based on the second paragraph of §112.

New claims 15 and 16 have been added which set forth the claimed invention in a slightly different way and thus avoid the criticism of the aforementioned rejection. Claims 15 and 16 are patentable for the same reasons as claim 1, as pointed out below.

Claims 1-14 have been rejected as obvious under §103 from Matsuo et al USP 4,472,503 (Matsuo) in view of Huang et al USP 5,418,147 (Huang) and Magda USP 5,763,172 (Magda). This rejection is respectfully traversed.

Applicants respectfully maintain that the cited and applied prior documents are individually and collectively quite different from applicants' claimed invention. Thus, even if the proposed combination were obvious (not conceded by applicants), collectively they do not reach the claimed invention for reasons pointed out below.

Huang describes in general the purification and characterization of phospholipase D. Magda describes the use of metallotexaphyrin complexes for the hydrolytic cleavage of ester bonds. Matsuo, the main and closest prior art, describes a method for enzymatic transesterification of a dry fatty acid substrate such as fats and oils of glycerides.

In more detail, the enzymatic method of Matsuo has the following essential requirements:

1. Matsuo makes use of a **dried medium** in the reaction:

> *After the enzyme-containing material is dispersed, absorbed or bonded in or to the carrier in an aqueous system, the resulting mixture is dried"* (column 6, lines 7-10).

2. Matsuo makes use of a **dried substrate** which thus cannot form a liposome:

> *The fatty acid substrate... should be dried... the total amount of water... should be maintained at a solubility limit of water in the fatty ester used or below."* (column 7, lines 52-60)

3. Matsuo makes use of an **essentially aqueous free environment** throughout the process:

> *Under these circumstances, it is required to carry out the enzymatic transesterification in a reaction mixture having a low water contents such as 0.18% or less in order to obtain a lipid in high quality...."* (column 2, lines 43-45)

> *The present inventors have surprisingly found that an enzyme preparation having transesterification activities is increased in effectiveness by continuously or repeatedly using the preparation in a dried reaction system,....* (column 2, lines 52-55).

Matsuo thus differs from the present invention in a fundamental way. The person of ordinary skill in the art,

reading Matsuo, cannot divert from Matsuo's key contribution. To state this another way, to proceed as applicants have done in an aqueous medium would be to fly in the face of Matsuo, the antithesis of obviousness.

Contrary to Matsuo and also contrary to Matsuo modified as proposed in the rejection by Huang and Magda, the present invention concerns a method which involves dissolving an enzyme in **an aqueous medium** containing a **liposomal suspension** of a phospholipids and a **hydroxyl containing reagent**, and adding silica gel to the medium, followed by agitation.

There are several features which make the instant method substantially different and non-obvious from the methods taught by the cited prior art:

- The use in the present invention of an **aqueous medium**;
- The use in the present invention of a **liposomal suspension**;
- The use in the present invention of **hydroxyl containing reagent** (such as water);
- The use in the present invention of silica gel **only after mixing the enzyme with the substrate**.

On this last point, it should be noted that Matsuo makes use of a solid carrier **before** the enzyme is mixed with the substrate.

> *After the enzyme-containing material is dispersed, adsorbed or bonded in or to the carrier in an aqueous system....* (column 6, lines 7-10)

Applicants' specification details the significance of each of the above features, particularly for large scale production. For example, the significance of using a liposomal suspension is detailed in Example F.

Since liposomes need an aqueous environment to be produced, the prior art methods could not have taught, and even teach away from, the conditions required to perform the method of the instant invention.

Huang and Magda have not been applied to make up for the aforementioned deficiencies of Matsuo, and indeed they do not do so. Therefore, even if the proposed combination were obvious, the resultant reconstruction of such a combination would not correspond to what is called for in applicants' main claims 1 and 15.

Withdrawal of the rejection is in order and is respectfully requested.

Applicants believe that all issues have been addressed and resolved above, and therefore applicants respectfully request favorable reconsideration and allowance.

Respectfully submitted,

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